REMARKS/ARGUMENTS

Reconsideration and continued examination of the above-identified application are respectfully requested.

By way of this amendment, claims 3, 4, and 17 have been canceled. Claim 1 has been amended to encompass an assay method for drug glucuronidation of UDP-glucuronosyltransferase (UGT) and to include the limitations of claims 3 and 4. Full support for the amendment can be found throughout the present application and the claims as originally filed. Claim 13 has been amended to specify that a detection device in which probes having a base sequence set forth in SEQ ID NO:1 and probes having a base sequence set forth in SEQ ID NO:2 and/or 3 are provided within the same device. Full support for the amendment can be found throughout the present application and the claims as originally filed, particularly, at pages 11-13 and page 15, lines 20-23 of the present application. Claims 20-21 have been newly added. The non-elected claims have been maintained for petition/appeal options, which is an appropriate option. Accordingly, no questions of new matter should arise and entry of the amendment is respectfully requested.

Rejection of Claims 1-3, 5-6, 13, and 17 under 35 U.S.C. §112 – First Paragraph

Beginning at page 4 of the Office Action and continuing to page 7, the Examiner states that claims 1-3, 5-6, 13, and 17 are rejected under 35 U.S.C. §112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the art that the inventor(s) had possession of the claimed invention. The Examiner asserts that the present claims encompass a number of variants, polymorphisms, and mutations for which no written description is provided in the specification and for which no common structural attributes have been identified. The Examiner asserts that a description of

only one member of the claimed genus is not representative of the variants of the genus and is insufficient to support the claim. The Examiner asserts that the general knowledge in the art concerning variants does not provide any indication of how the structure of one allele is representative of unknown alleles. The Examiner also asserts that the polymorphisms shown are not representative of the genus of any polymorphism associated with drug metabolizing activity of UGT because it is not clear which polymorphisms in the UGT nucleic acid would have the same effect. The Examiner states, however, that the specification provides data for the polymorphism in exon 5, namely 1456 TAC-GAC, also designated Tyr486Asp. This rejection is respectfully traversed.

Applicants respectfully point out that the previous claims and present claims fully comply with the requirements of 35 U.S.C. §112, first paragraph. Claim 1 specifies that the mutation which is to be detected corresponds to nucleotide number 1456 in the genetic sequence of UGT which encodes an amino acid at position 486 in the amino acid sequence of UGT1A1. As acknowledged by the Examiner, the present application provides adequate support for this particular mutation. Applicants also point out that claim 13, as presently amended, recites the use of probes for assessing, predicting, or assaying drug metabolism and specifically identifies the base sequences for the probes. Claims 3 and 17 have been canceled. Accordingly, the rejection should be withdrawn.

Rejection of Claims 1-6, 10, 13, 17, and 19 under 35 U.S.C. §112, first paragraph -- Enablement

Beginning at page 7 of the Office Action and continuing to page 12, the Examiner states that claims 1-6, 10, 13, 17, and 19 are rejected under 35 U.S.C. §112, first paragraph, as failing to comply with the enablement requirement. The Examiner asserts that the present invention is

in a class characterized as "the unpredictable arts such as chemistry and biology." According to the Examiner, Hirschhorn et al. (Genetics in Medicine, Vol. 4, No. 2, pages 45-61, March 2002) teaches that most genetic variations and associations are irreproducible. Accordingly, the Examiner indicates that use of association studies for diagnostics and prognostics should be considered with caution. The Examiner further asserts that Ioannidis (Nature Genetics, Vol. 29, pages 306-309, November 2001) teaches that the results of a first association study correlate only modestly with subsequent research on the same association. The Examiner, relying on Meyer et al. (PG Pub. 2003/0092019), also asserts that the association of a single SNP in a gene does not indicate that all SNPs within that gene are associated with the disease.

The Examiner asserts that the quantity of experimentation is extremely large since there are a number of parameters which would have to be studied. The Examiner points out that the claims are drawn to any exon 5 mutation while the specification teaches a single mutation in exon 5 of the UGT gene. The Examiner also points out that the claims are drawn to any drug metabolizing activity. According to the Examiner, the specification teaches that UGT enzymes catalyze glucuronidation of various drugs. The Examiner asserts that the specification analyzes a single drug which is glucuronidated by UGT. The Examiner concludes that the skilled artisan would be required to perform undue experimentation to practice the scope of the claimed invention. The rejection is respectfully traversed.

Claim 1 recites "...assay method for drug glucuronidation... ." Claim 1 sufficiently defines the type of drug metabolizing activity and the exon 5 mutation recited in the claims. Applicants respectfully submit that the specification enables one skilled in the art to practice the scope of the previous claims and present claims without undue experimentation. The rejection should be withdrawn.

Rejection of Claims 1-6, 10, 17, and 19 under 35 U.S.C. §112, second paragraph -- Indefiniteness

At the top of page 12 of the Office Action, the Examiner states that claims 1-6, 10, 17, and 19 are rejected under 35 U.S.C. §112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The Examiner states that claims 1-6, 10, 17, and 19 are indefinite because it is unclear whether the method is drawn to an assay for drug metabolizing activity of UGT or a method for detecting a mutation in exon 5 region of a gene coding for UGT. The applicants respectfully traverse this rejection.

The present application discloses that one can predict drug metabolism by detecting a mutation in the exon 5 region of a gene coding for UGT, (page 3, line 23-page 4, line 2) (page 8, lines 12-17). Thus, the present application makes clear that an assay method for drug metabolizing activity of UGT, according to the present invention, comprises a step of detecting a mutation in the exon 5 region of a gene coding for UGT. The claims are drawn to an assay method for drug glucuronidation of UGT, comprising a step of detecting a mutation in an exon 5 region. Accordingly, the rejection should be withdrawn.

Rejection of Claims 1-6 and 17 under 35 U.S.C. §102 (b) -- Huang et al.

At the bottom of page 12 of the Office Action, the Examiner states that claims 1-6 and 17 are rejected under 35 U.S.C. §102 (b), as being anticipated by Huang et al. (Pharmacogenetics, Vol. 10, pages 539-544, 2000). The Examiner states that this rejection is applied because it is unclear whether the method is for drug metabolizing activity of UGT or a method for detecting mutations in an exon 5 region of a gene coding for UGT, as discussed previously. The Examiner

states that Huang et al. teaches variations of the bilirubin uridine-diphosphoglucuronosyl transferase 1A1 gene in healthy Taiwanese individuals. The Examiner states that Huang et al. teaches that activity of UGT1 may influence the concentration of serum bilirubin. Huang et al. teaches a variation site in UGT1A1 gene in exon 5, at nucleotides 1456 which is a TAC to GAC substitution which corresponds to the amino acid substitution Tyr486Asp (page 541). Applicants respectfully traverse this rejection.

As pointed out previously, the claims are drawn to an assay method for drug glucuronidation of UGT, comprising a step of detecting a mutation in an exon 5 region. The present application makes clear that an assay method for drug metabolizing activity of UGT, according to the present invention, comprises a step of detecting a mutation in the exon 5 region of a gene coding for UGT (page 3, line 23-page 4, line 2) (page 8, lines 12-17). Applicants respectfully point out that while Huang et al. teaches analyzing serum bilirubin levels for variants, Huang et al. does not teach "an assay method for drug glucuronidation of UGT." Furthermore, Huang et al. fails to provide any teaching relating to isoforms of UGT1. Accordingly Applicants respectfully request the Examiner to withdraw this rejection.

Rejection of Claims 1, 3, 4, 13, and 17 under 35 U.S.C. §102(b) – Ito et al.

At page 13 of the Office Action, the Examiner states that claims 1, 3, 4, 13, and 17 are rejected under 35 U.S.C. §102(b) as being anticipated by Ito et al. (Eur. J. Clin. Pharmacol. Vol. 58, pages 11-14, February 16, 2002). The Examiner states that Ito et al. teaches that patients with a Y486D mutation in UGT1A1 may accumulate excessive 2-amino-5-nitro-4-trifluoromethylphenol, which might lead to unexpected toxicity. The Examiner states that Ito et al. also teaches that the mutation corresponding to Y486D of UGT1A1 is conserved in all UGT1

isoforms (page 13, col. 1). Applicants respectfully traverse this rejection.

Ito et al. is an inappropriate reference under 35 U.S.C. §102(b) in view of the priority date of the present application. Applicants note that the publication date of Ito et al. is February 16, 2002, which is within one year of the priority date of the present application, August 12, 2002. Applicants submit herewith a certified English translation of the Japanese priority application which further establishes that Applicants are entitled to the priority date of August 12, 2002.

Applicants also point out that Ito et al. is an inappropriate reference under 35 U.S.C. §102(a). The Ito et al. reference is subject matter that was conceived and invented by the present inventors, Hiroshi Sato, Yoshihide Fujiyama, and Kazuo Yamamoto. Applicants submit that Masaki Ito, Yoshihiro Maruo, and Tadao Bamba were lab assistants working under the present inventors and were involved in the preparation of the Ito et al. publication. In view of their contributions in preparing the Ito et al. publication, the present inventors acknowledged their assistance by naming them in the Ito et al. publication. However, Masaki Ito, Yoshihiro Maruo, and Tadao Bamba were not named as inventors of the present application because their contributions were not of an inventive nature. Applicants will be filing a declaration from the inventors shortly to further confirm these points. Accordingly, Applicants respectfully request the Examiner to withdraw this rejection.

Rejection of Claims 1, 3, 4, 13, and 17 under 35 U.S.C. §102 (a) – Gagne et al.

At page 14 of the Office Action, the Examiner states that claims 1, 3, 4, 13, and 17 are rejected under 35 U.S.C. §102 (a) as being anticipated by Gagne et al. (Molecular Pharmacology, Vol. 62, No. 3, pages 608-617, August 16, 2002). The Examiner states that Gagne teaches

common human UGT1A polymorphisms and the altered metabolism of irinotecan active metabolite 7-ethyl-10-hydroxycamptothecin (SN-38). The Examiner asserts that Gagne teaches analyzing the functional effect of known common allelic variations of UGT1A isoenzymes involved in SN-38G formation including Y486. The Examiner states that Gagne teaches an important decrease in SN-38-G formation was observed for the UGT1A1*7 variant. The Examiner states that Applicant cannot rely on the Japanese priority application to overcome this rejection because a translation of the papers has not yet been filed. This rejection is respectfully traversed.

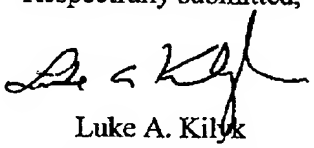
The cited Gagne reference was published on August 16, 2002, while the present application claims the benefit of the August 12, 2002 Japanese filing date. As mentioned previously, Applicants submit herewith a certified English translation of the Japanese priority application to further establish Applicants' entitlement to the claimed priority date. In view of the priority date of the present application, Applicants respectfully submit that Gagne et al. does not constitute prior art with respect to the present application. Accordingly, withdrawal of this rejection is respectfully requested.

CONCLUSION

In view of the foregoing remarks, the applicant respectfully requests the reconsideration of this application and the timely allowance of the pending claims.

If there are any fees due in connection with the filing of this response, please charge the fees to our Deposit Account No. 50-0925. If a fee is required for an extension of time under 37 C.F.R. § 1.136 not accounted for above, such extension is requested and should also be charged to said Deposit Account.

Respectfully submitted,



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